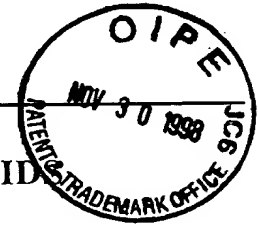


US Patent Application No. 09/101,825  
Steen Research Group A/S  
Synthetic IL-10 analogues  
Your ref: GRONHOJ-LARSEN=2  
Our ref: 17705 US 1



List of references for preparation of IDS

FH

1. Bendtzen K. Lymphokines in inflammation. Inflammation Basic Mechanisms Tissue Injuring Principles and Clinical Models (P Venge & A Lindbom eds) 1985; Almquist & Wiksell International. Stockholm: 187-217.
2. Bendtzen K. Interleukin-1, Interleukin-6, and tumor necrosis factor in infection, inflammation and immunity. Immunol Lett 1988;19:183-192.
3. Larsen C.G. Leukocyte activating and chemotactic cytokines in cell-mediated immune reactions of the human skin. Acta Dermatovenereol. 1991; Suppl. 160:1-48
4. Fiorentino D. F., M. W. Bond, and T. R. Mosmann. 1989. Two types of mouse helper T cell. IV. Th2 clones secrete a factor that inhibits cytokine production by Th1 clones. J. Exp. Med., 170:2081.
5. Viera P., R. de Wall-Malefyt, M.-N. Dang, K. E. Johnson, R. Kastelein, D. F. Fiorentino, J. E. de Vries, M.-G. Roncarolo, T. R. Mosmann, and K. W. Moore. 1991. Isolation and expression of human cytokine synthesis inhibitory factor (CSIF/IL-10) cDNA clones: homology to Epstein-Barr virus open reading frame BCRF1. Proc. Natl. Acad. Sci. (USA), 88:1172.
6. Moore, K.W., O'Garra A., de Waal Malefyt R., Vieira, Mosmann T.R. 1993. Interleukin-10, Annu Rev. Immunol, 11:165-90.
7. Kim, J.M., Brannan, C.I. Copeland N.G., Jenkins, N.A., Khan, T.A., Moore, K.W. 1992. Structure of the mouse interleukin-10 gene and chromosomal localization of the mouse and human genes. J. Immunol 148:3618-23.
8. Carter, D.B., Deibel, M.R.-Jr, Dunn, C.J. et al. 1990. Purification, cloning, expression and biological characterization of an interleukin-1 receptor antagonist protein. NATURE 344:633-638.
9. Hannum, C.H., Wilcox, C.J., Arend, W.P. et al. 1990. Interleukin-1 receptor antagonist activity of a human interleukin-1 inhibitor. Nature 343:336-40.
10. Firestein, G.S., Boyle, D.L., Yu, C., et al. 1994. Synovial interleukin-1 receptor antagonist and interleukin-1 balance in rheumatoid arthritis. Arthritis Rheum 37:644-652.
11. Fisher, C.J.-Jr., Slotman, G.J., Opal, S.M., Pribble, J.P. et al. 1994. Initial evaluation of recombinant interleukin-1 receptor antagonist in the treatment of sepsis syndrome: a randomized, open-label, placebo-controlled multicenter trial. The IL-1RA Sepsis Syndrome Study Group. Crit-Care-Med. 22:12-21.
12. de Waal-Malefyt, R., Haanen J., Spits, H., et al. 1991. IL-10 and viral IL-10 strongly reduce antigen-specific human T cell proliferation by diminishing the antigen-presenting capacity of monocytes via down-regulation of class II MHC expression. J. Exp. Med. 174:915-24.

Consolidated on

3/22/00

For H. and

FH

13. Gazzinelli, R.T., Oswald, I.P., James, S.L., Sher, A., 1992. IL-10 inhibits parasite killing and nitric oxide production by IFN- $\gamma$ -activated macrophages. *J. Immunol.* 148:1792-96.
14. Jinquan, T., Larsen, C.G., Gesser, B., Matsushima, K., Thestrup-Pedersen, K. 1993. Human IL-10 is a chemoattractant for CD8+ T lymphocytes and an inhibitor of IL-8- induced CD4+ T lymphocyte Migration. *Journal of Immunology*, 151:4545-4551.
15. Rousset F., E. Garcia, T. Defrance, C. Peronne, D.-H. Hsu, R. Kastelein, K. W. Moore, and J. Banchereau. 1992. IL-10 is a potent growth and differentiation factor for activated human B lymphocytes. *Proc. Natl. Acad. Sci. USA*, 175:671.
16. Howard, M., O'Garra, A., Ishida, H., de Waal Malefyt, R., de Vries, J. 1992. Biological properties of Interleukin-10. *J. Clin. Immunol* 12:239-47.
17. Kuhn, R., Lohler, J., Rennick, D., Rajewsky, K., Muller, W. 1993. Interleukin-10-deficient mice develop chronic enterocolitis. *Cell* 75: 263-74.
18. Sher, A., Fiorentino, D.F., Caspar, P., Pearce, E., Mosmann, T. 1991. Production of IL-10 by CD4+ lymphocytes correlates with down-regulation of Th1 cytokine synthesis in helminth infection. *J. Immunol.* 147:2713-16.
19. Clerici, M., Shearer, G.M. 1993 *Immunology Today*. 14:107-111.
20. Bry, K., Lappalainen, U. 1994. Interleukin-4 and transforming growth factor-beta 1 modulate the production of interleukin-1 receptor antagonist and prostaglandin E2 by decidual cells. *Am-J-obstet-Gynecol* 170 (4): 1194-1198
21. Roberge, C. J., De-Medicis, R., Dayer, J. M., Rola-Pleszczyczynski, M., Naccahe, P. H., Poubelle, P. E. 1994. Crystal-induced neutrophil activation: V. Differential production of biologically active IL-1 receptor antagonist. *J. Immunol* 152/11: 5485-5494
22. McCall, R. D., Haskill, S., Zimmermann, E. M., Lund, P. K., Thompson, R. C., Sartor, R. B. 1994. Tissue interleukin 1 and interleukin-1 receptor antagonist expression in enterocolitis in resistant and susceptible rats. *Gastroenterology* (4): 960-72
23. Kimble, R. B., Vannice, J. L., Bloedow, D. C., Thompson, R. C., Hopfer, W., Kung, V. T., Brownfield, C., Pacifici, R. 1994. Interleukin-1 receptor antagonist decreases bone loss and bone resorption in ovariectomized rats. *J. Clin Invest.* 93/5: 1959-1967
24. Kline, J. N., Geist, L. J., Monick, M. M., Stinski, M. F., Hunninghake, G. W., 1994. *J. Immunol.* 152 (5): 2351-7
25. Tompkins, R. G. 1994. Human recombinant interleukin-1 receptor antagonist in the treatment of sepsis syndrome (editorial; comment). *Crit-Care-Med.* 22 (1): 3, 22 (1):12-21
26. Everaerd, B., Brouckaert, P., Fiers, W. 1994. Recombination IL-1 receptor antagonist protects against TNF-induced lethality in mice. *J. Immunol.* 152/10: 5041-5049
27. Fischer, C. J. Jr., Slotman, G. J., Opal, S. M., Pribble, J. P., Bone, R. C., Emmanuel, G., Ng, D., Bloedow, D. C., Catalano, M. A. 1994. Initial evaluation of human recombination interleukin-1 receptor antagonist in the treatment of sepsis syndrome: a randomized, open-label, placebo-controlled multicenter

For Howard considered on 3/22/00

trial. The IL-1RA Sepsis Syndrome Study Group (see comments). Crit-Care-Med. 22(1): 12-21, 22(1): 3

28. Gomez-Reino-Carnoto, J. J. 1994. New therapies in rheumatoid arthritis. Med-Clin 543-545. *English translation in Paper #5 Filed on 2/25/99*
29. Nishihara, T., Ohsaki, Y., Ueda, N., Saito, N., Mundy, G. R. 1994. Mouse interleukin-1 receptor antagonist induced by actinobacillus actinomycetem-comitans lipopolysaccharide blocks the effects of interleukin-1 on bone resorption and osteoclast-like cell formation. Infect-Immun. 62(2): 390-7
30. Simon, C., Frances, A., Piquette, G. N., el-Danasouri, I., Zurawski, G., Dang, W., Polan, M. L. 1994. Embryonic implantation in mice is blocked by interleukin-1 receptor antagonist (see comments). Endocrinology. 134(2): 521-8, 134(2): 519-20
31. Baergen, R., Benirschke, K., Ulich, T. R., 1994. Cytokine expression in the placenta. The role of interleukin 1 and interleukin 1 receptor antagonist expression in chorioamnionitis and parturition. Arch-Pathol-Lab-Med. 118(1): 52-5
32. Tang, W.W., Feng, L., Vannice, J. L., Wilson, C. B. 1994. Interleukin-1 receptor antagonist ameliorates experimental antglomerular basement membrane antibody-associated glomerulonephritis. J. Clin-Invest. 93(1): 279-9.
33. Cassatella, M. A., Meda, L., Gasperini, S., Calzetti, F., Bonara, S. 1994. Interleukin 10 (IL-10) upregulates IL-1 receptor antagonist production from lipopolysaccharide-stimulated human polymorphonuclear leukocytes by delaying mRNA degradation. J. Exp-Med. 179/5: 1695-1699
34. Mancini, R., Bendetti, A., Jezequel, A. M. 1994. An interleukin-1 receptor antagonist decreases fibrosis induced by dimethylnitrosamine in rat liver. Virchows-Arch. 424/1: 25-31
35. Lukacs, N. W., Kunkel, S. L., Burdick, M. D., Lincoln, P. M., Strieter, R. M. 1993. Interleukin-1 receptor antagonist blocks chemokine production in the mixed lymphocyte reaction. Blood. 82(12): 3668-74
36. Bandara, G., Mueller, G. M., Galea-Lauri, J., Tindal, M. H., Georgescu, H. I., Suchanek, M. K., Hung, G. L., Gloriso, J. C., Robbins, P. D., Evans, C. H. 1993. Intraarticular expression of biologically active interleukin 1-receptor-antagonist protein by ex vivo transfer. Proc-Natl-Acad-Sci-U-S-A. 90(22): 10764-8
37. Dinarello, C. A. 1994. Anti-interleukin-1 strategies in the treatment of the septic shock syndrome. Can-J-infect-Dis. 5(suppl. A): 9A-16A
38. Oelmann, E., Topp, M. S., Reufi, B., Papadimitriou, C., Koeningsmann, M., Oberberg, D., Thiel, E., Berdel, W. E. 1994. Int-J-Oncol. 4/3: 555-558
39. Estrov, Z. 1993. Interruption of autocrine and paracrine growth-stimulatory mechanisms: a new therapeutic strategy for chronic myelogenous leukemia. Semin-Hematol. 30(3 suppl 3): 35-6
40. Wooley, P.H., Whalen, J.D., Chapman, D.L., Berger, A.E., Richard, K.A., Aspar, D.G., Staite, N.D. 1993. The effect of an interleukin-1 receptor antagonist protein on type II collagen-induced arthritis and antigen-induced arthritis in mice. Arthritis Rheum. 36 (9): 1305-1314
41. Peterson, C.M., Hales, H.A., Hatasaka, H.H., Mitchell, M.D., Rittenhouse, L., Jones, K.P. 1993. Interleukin-1 beta (IL-1 beta) modulates prostaglandin

for H → considered on 3/22/00

production and the natural IL-1 receptor antagonist inhibits ovulation in the optimally stimulated rat ovarian perfusion model. *Endocrinology* 133 (5): 2301-2306

- Fit ✓
- ✓ 42. Estrov, Z., Kurzrock, R., Talpaz, M. 1993. Role of interleukin-1 inhibitory molecules in therapy of acute and chronic myelogenous leukemia. *Leuk. Lymphoma* 10 (6): 407-418
- ✓ 43. Chensue, S.W., Bienkowski, M., Eessalu, T.E., Warmington, K.S., Hershey, S.D., Lukacs, N.W., Kunkel, S.L. 1993. The IL-1 receptor antagonist protein (IRAP) regulates schistosome egg granuloma formation and the regional lymphoid response. *J. Immunol.* 151 (7): 3654-3662
- ✓ 44. Bowyer, J.F., Davies, D.L., Schmued, L., Broening, H.W., Newport, G.D., Slikker, W Jr., Holson, R.R. 1994. Further studies of the role of hyperthermia in methamphetamine neurotoxicity. *J. Pharmacol. Exp. Ther.* 268/3: 1571-1580
- ✓ 45. Cole, O.F., Sullivan, M.H.F., Elder, M.G. 1993. The 'interleukin-1 receptor antagonist' is a partial agonist of prostaglandin synthesis by human decidual cells. *Prostaglandins* 46/6: 493-498
46. Jenkins, J.K., Arend, W.P. 1993. Interleukin 1 receptor antagonist production in human monocytes is induced by IL-1 $\alpha$ , IL-3, and IL-4 and GM-CSF. *Cytokine* 5/5: 407-415
- ✓ 47. Coceani, F., Lees, J., Redford, J., Bishai, I. 1992. Interleukin-1 receptor antagonist: effectiveness against interleukin-1 fever. *Can. J. Pharmacol.* 70 (12): 1590-1596
- ✓ 48. Schiro, R., Longoni, D., Rossi, V., Maglia, O., Doni, A., Arsura, M., Carrara, G., Masera, G., Vannier, E., Dinarello, C.A., Rambaldi, A., Biondi, A. 1994. Suppression of juvenile chronic myelogenous leukemia colony growth by interleukin-1 receptor antagonist. *Blood* 83/2: 460-465
- ✓ 49. Watson, M.L., Smith, D., Bourne, A.D., Thompson, R.C., Westwick, J. 1993. Cytokines contribute to airway dysfunction hyperreactivity, pulmonary eosinophil accumulation and tumor necrosis factor generation by pre-treatment with an interleukin-1 receptor antagonist. *Am. J. Respir. Cell Mol. Biol.* 8 (4): 365-369
- ✓ 50. Abhyankar, S., Gilliland, D.G., Ferrara, J.L.M. 1993. Interleukin-1 is a critical effector molecule during cytokine dysregulation in graft-versus-host disease to minor histocompatibility antigens. *Transplantation* 56/6: 1518-1523
- ✓ 51. Lan, H.Y., Nikolic Paterson, D.J., Zarama, M., Vannice, J.L., Atkins, R.C. 1993. Suppression of experimental crescentic glomerulonephritis by the interleukin-1 receptor antagonist. *Kidney Int.* 43 (2): 479-485
- ✓ 52. Herve, P. 1993. Prevention and treatment of acute GvHD - New modalities. *Nouv. Rev. Fr. Hematol.* 35/3: 295-297
- ✓ 53. Conti, P., Panara, M.R., Barbacane, R.C., Placido, F.C., Bongrazio, M., Reale, M., Dempsey, R.A., Fiore, S. 1992. Blocking the interleukin-1 receptor inhibits leukotriene B4 and prostaglandin E2 generation in human monocyte cultures. *Cell Immunol.* 145 (1): 199-209
- ✓ 54. Kristensen, M., Deleuran, B., Eedy, D.J., Feldmann, M., Breathnach, S.M., Brennan, F.M. 1992. Distribution of interleukin-1 receptor antagonist protein (IRAP), interleukin-1 receptor, and interleukin-1  $\alpha$  in normal and psoriatic

For H and considered 3/22/00

- skin, Decreased expression of IRAP in psoriatic lesional epidermis. *Br. J. Dermatol.* 127 (4): 305-311
- FI4 ✓ 55. Romero, R., Sepulveda, W., Mazor, M., Brandt, F., Cotton, D.B., Dinarello, C.A., Mitchell, M.D. 1992. The natural interleukin-1 receptor antagonist in term and pre-term parturition. *Am. J. Obstet. Gynecol.* 167 (4 Pt 1): 863-872
- ✓ 56. Dinarello, C.A. 1992. Reduction of inflammation by decreasing production of interleukin-1 or by specific receptor antagonism. *Int. J. Tissue. React.* 14 (2): 65-75
- ✓ 57. Conti, P., Panara, M.R., Barbacane, R.C., Bongrazio, M., Dempsey, R.A., Reale, M. 1993. Human recombinant IL-1 receptor antagonist (IL-1Ra) inhibits leukotriene B4 generation from human monocyte suspensions stimulated by lipopolysaccharide (LPS). *Clin. Exp. Immunol.* 91/3: 526-531
- ✓ 58. DeForge, L.E., Tracey, D.E., Kenney, J.S., Remick, D.G. 1992. Interleukin-1 receptor antagonist protein inhibits interleukin-8 expression in lipopolysaccharide-stimulated human whole blood. *Am. J. Pathol.* 140 (5): 1045-1054
- ✓ 59. Porat, R., Poutsika, D.D., Miller, L.C., Granowitz, E.V., Dinarello, C.A. 1992. Interleukin-1 (IL-1) receptor blockade reduces endotoxin and Borreliaburgdorferi-stimulated IL-8 synthesis in human monoclear cells. *Faseb. J.* 6 (7): 2482-2486
- ✓ 60. Boermeester, M.A., van Leeuwen, P.A.M., Schneider, A.J., Houdijk, A.P.J., Ferwerda, C.C., Wesdorp, R.I.C. 1993. Interleukin-1 receptor antagonist: A new therapeutic agent in the treatment of septic syndrome. *Ned. Tijdschr. Geneesks.* 137/7: 337-342
- ✓ 61. Smith, R.J., Chin, J.E., Sam, L.M., Justen, J.M. 1991. Biologic effects of an interleukin-1 receptor antagonist protein on interleukin-1-stimulated cartilage erosion and chondrocyte responsiveness. *Arthritis Rheum.* 34 (1): 78-83
- ✓ 62. Conti, P., Barbacane, R.C., Panara, M.R., Reale, M., Placido, F.C., Fridas, S., Bongrazio, M., Dempsey, R.A. 1992. Human recombinant interleukin-1 receptor antagonist (hrIL-1ra) enhances the stimulatory effect of interleukin-2 on natural killer cell activity against MOLT-4 target cells. *Int. J. Immunopharm.* 14/6: 987-993
- ✓ 63. Selig, W., Tocker, J. 1992. Effect of interleukin-1 receptor antagonist on antigen-induced pulmonary responses in guinea pigs. *Eur. J. Pharmacol.* 213/3: 331-336
- ✓ 64. McCarthy, P.L. Jr., Abhyankar, S., Neben, S., Newman, G., Sieff, C., Thompson, R.C., Burakoff, S.J., Ferrara, J.L.M. 1991. Inhibition of interleukin-1 by an interleukin-1 receptor antagonist prevents graft-versus-host diseases. *Blood* 78/8: 1915-1918
- ✓ 65. Estrov, Z., Kurzrock, R., Wetzler, M., Kantarjian, H., Blake, M., Harris, D., Gutterman, J.U., Talpaz, M. 1991. Suppression of chronic myelogenous leukemia colony growth by interleukin-1 (IL-1) receptor antagonist and soluble IL-1 receptors: A novel application for inhibitors of IL-1 activity. *Blood* 78/6: 1476-1484
- ✓ 66. Thomas, T.K., Will, P.C., Srivastava, A., Wilson, C.L., Harbison, M., Little, J., Chesonis, R.S., Pignatello, M., Schmolze, D., Symington, J., Kilin, P.L.,

for hand considered on  
3/22/00

Thompson, R.C. 1991. Evaluation of an interleukin-1 receptor antagonist in the rat acetic acid-induced colitis model. Agents Actions 34/1-2: 187-190

67. Carter, D.B., Deibel, M.R. Jr., Dunn, C.J., Tomich, C.S.C., Laborde, A.L., Slightom, J.L., Berger, A.E., Bienkowski, M.J., Sun, F.F., McEwan, R.N., Harris, P.K.W., Yem, A.W., Waszak, G.A., Chosay, J.G., Sieu, L.C., Hardee, M.M., Zurcher Neely, H.A., Reardon, I.M., Heinrikson, R.L. et al. 1990. Purification, cloning expression and biological characterization of an interleukin-1 receptor antagonist protein. Nature 344/6267: 633-638
68. Larsen C.G., Anderson A.O., Apella E., Oppenheim J.J., Matsushima K., 1989. Science 243:1464;
69. Larsen C.G., Jinquan T., Deleurant B., Thestrup-Pedersen K. 1993, IL-10 is a potent regulator of the chemotactic response of mononuclear cells, but not of granulocytes. J. Invest. Dermatol. Vol 100, No 6
70. Sankoff and Kruskal in chapter 1 of "Time Warps, String Edits, and Macromolecules: The Theory and Practice of Sequence Comparison" (Addison-Wesley, Reading, Mass 1983).
71. Berzofsky, Science 229, (1985) 932-940
72. Bowie et al., Science 247, (1990) 1306-1310
73. Wasserman et al., J. Immunol. 87, 1961, 290-295
74. Levine et al., Methods in Enzymology 11, 1967, 928-936
75. Lewis et al., Biochemistry 22, 1983, 948-954
76. Rene de Waal Maletyt, John Abrahams, Bruce Bennet, Carl G. Figdor and Jan E. de Vries (1991), Interleukin 10 (IL-10) Inhibits Cytokine Synthesis by Human Monocytes: An Autoregulatory Role of IL-10 Produced by Monocytes. J. Exp. Med. 174, 1209-1220
77. Szoka et al., Ann. Rev. Biophys. Bioeng. 9, 1980, 467
78. US 4,235,871
79. US 4,501,728
80. US 4,837,028.
81. Walter H. Gotlieb, John S. Abrams, Joanna M. Watson, Thierry J. Velu, Jonathan S. Berek, Otniel Martinez-Meza (1992), Presence of interleukin 10 (IL-10) in the ascites of patients with ovarian and other intra-abdominal cancers. Cytokine 4, No. 5, 385-390
82. Blanco G., P. Gianello, Sh. Germana, M. Baetscher, D.H. Sachs and Chr. LeGuern (1995), Molecular identification of porcine interleukin 10: Regulation of expression in kidney allograft model. Proc. Natl. Acad. Sci. USA 92, 2800-2804
83. Howard, M., T. Muchamuel, S. Andrade, S. Menon (1993), Interleukin 10 protects mice from lethal endotoxemia. J. Exp. Med. 177, 1205-1208

For Howard 3/22/00

84. Chernoff, A.E., E.V. Granowitz, L. Shapiro, E. Vannier, G. Lonnemann, J.B. Angel, J.S. Kennedy, A.R. Rabson, S. Wolff, C.A. Dinarello (1995), A randomized, controlled trial of IL-10 in humans. Inhibition of inflammatory cytokine production and immune responses. *J. Immunol.* 154, 5492-5499
85. Banerjee, A.K., S.W. Galloway and A.N. Kingsnorth (1994), Experimental models of acute pancreatitis. *Br. J. Surg.* 81, 1096-1103
86. Hong, S.S., D.S. Chin, T.S. Cho, S.E. Kim (1962), Experimental pancreatitis induced by alcohol and bile in rabbits. *Annals of Surgery* 156(6), 929-939
87. Pelton, J.T., et al., *Proc. Natl. Acad. Sci. USA* 82, 233-239
88. Dyson, H., et al. (1988), *Annual Review of Biophysics and Biophysical Chemistry* 17, 305-324.
89. Nakanishi, H., et al. (1993), Peptidomimetics of the immunoglobulin supergene family - a review. *Gene* 137, 51-56
90. US 5,446,128
91. Walter et al. (1995), *Biochemistry* 34, 12118-25
92. Marshall, G.R. (1993), *Tetrahedron* 49, 3547-3558
93. Merrifield, R.B. (1963), *J. Amer. Chem. Soc.* 85, 2149-2154
94. Kent, S.B.H. (1988), *Annu. Rev. Biochem.* 57, 957-989
95. Carpino, L.A. and Han, G.Y. (1972), *J. Org. Chem.* 37, 3404-3409
96. Ikeda, N. et al. (1995), *Infection and Immunity*, 4812-4817
97. Fink, G.W. and Norman, J.G. (1996), "Intrapancreatic Interleukin-1 $\beta$  Gene Expression by Specific Leukocyte Populations during Acute Pancreatitis", *J. Surgical Research* 63, 369-373
98. Gaur, D. et al. (1996), "Phylogenetic position of the order Lagomorpha (rabbits, hares and allies)", *Nature*, 379, 333-335
99. Poli, G. et al. (1994), *Proc. Natl. Acad. Sci. USA* 91, 108-112
100. Jensen, I.M. et al. (1993), *Analyt. Cell. Pathol.* 5, 213-223
101. Berman, R.M., Suzuki, T. et al. (1996), "Systemic administration of cellular IL-10 induces an effective, specific, longlived immune response against established tumors in mice", *J. Immunol.* 157, 231-238
102. Zheng, L.M., Ojcius, D.M. et al. (1996), "IL-10 inhibits tumor metastasis through an NK cell-dependent mechanism", *J. Exp. Med.* 184, 579-584
103. Kundu, N., Beaty, T.L. et al. (1996), "Antimetastatic and anti-tumor activities of IL-10 in a murine model of breast cancer", *J. Natl. Cancer Inst.* 88, 479-480
104. Kollmann, T.R., Pettoello-Mantovani, M. et al. (1996), "Inhibition of acute in vivo HIV infection by human IL-10 treatment of SCID mice implanted with human fetal thymus and liver", *Proc. Natl. Acad. Sci. USA* 93, 3126-3131
105. Maini, R.N. (1996), "A perspective on anti-cytokine and anti T cell directed therapies in rheumatoid arthritis", *Clin. Exp. Rheumatol.* 13, suppl. 12, S35-40
106. WO 93/02693
107. WO 94/04180

References mentioned in International Search Report(copy enclosed),  
dated 3 September 1996

108. EP 0405980 (Schering corporation) Januar 1991

for H-and considered 3/22/00

Fit

109. WO 96/01318 (Nycomed Dak) Januar 1996

**References mentioned in International Search Report (copy enclosed), dated 21 April 1997**

EP 0405980 (Schering corporation) Januar 1991 (No. 108)

WO 96/01318 (Nycomed Dak) Januar 1996 (No. 109)

- 110. Gesser et al: Interleukin-8 induces its own formation in CD4+ T lymphocytes: a process regulated by Interleukin-10", Biochemical and Biophysical Research Communications, vol. 210, no. 3, 25 May 1995
- 111. N.K.Kootstra et al.: "Interference of interleukin-10 with human immunodeficiency virus type 1 replication in primary monocyte-derived macrophages", J. Virology, vol. 68, no. 11, November 1994
- 112. Van Laethem et al.: "Interleukin-10 prevents necrosis in murine experimental acute pancreatitis", pages 1917-1922, File Medline, abstract 95286011, 1995 XP002029903

considered 3/22/00  
for H and